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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,448	03/20/2002	Katy Drieu	00537-194002	4565

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 08/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/018,448

Applicant(s)

DRIEU ET AL.

Examiner

Gollamudi S. Kishore, Ph.D

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-24 and 26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-24 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5-19-05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 5-19-05 is acknowledged.

Claims included in the prosecution are 1-3, 5-24 and 26.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3, 5-24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro inhibition of MDA –231 cells by Ginkgolide B, does not reasonably provide enablement for the generic “a method of combating cancer by Ginkgolide B or Ginkgo biloba extracts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Cancer as is well known in the art is a generic term used for multitudes of different cell proliferative diseases and there is no specific drug which can be used to treat all forms of cancer. Just because a specific component is effective in the expression of a specific gene or effective in in vitro inhibition of a specific cancer cell cultures, one cannot draw a conclusion that either an extract containing that specific compound or the specific compound itself is effective in the in vivo treatment of various cancers. Instant specification lacks adequate description to come to that conclusion. Broad claims must have broad basis of support in the specification. In the absence of such support, claims

must be limited to the in vitro effectiveness of Ginkgolide B in inhibiting MDA-231 cells in culture.

Applicant's arguments have been fully considered, but are not found to be persuasive. The essence of applicant's arguments appear to be that a variety of cancers have been identified as having a dramatic increase in the number of peripheral-type benzodiazepine binding sites and Ginkgolide B binds to these receptors and therefore, it is effective against cancers. This argument is not persuasive since many components are affected in cancer cells, which may or may not be causative factors for the cells to become cancerous. Just because this compound reduces the breast tumor sizes of implanted breast cancer cells which express high amounts of these receptors does not necessarily mean that it is effective against all cancers since applicants have not established benzodiazepine receptors are causative factors. As applicants are aware there is high degree of unpredictability in terms of treatment of cancers even with art well-known anti-cancer agents such as taxanes and platinum complexes and it is a well-known fact that one cancer agent cannot effectively treat all types of cancers. The rejection is maintained.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3, 5-7, 16-24 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by DE 42 08 868 or EP 0 359 951 (both are of record).

DE 42 08 868 discloses a method of treatment of cancer using Ginkgo biloba extracts (abstract and col. 1 and claims).

Similarly EP discloses a method of treatment of cancer using Ginkgo biloba extracts (see entire patent).

The mechanism by which the composition of the prior art functions has no patentable significance since it is the inherent effect of the prior art extract.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that EP 951 teaches the usefulness of using a dry extract of Ginkgo biloba in conjunction with traditional cancer

Treatments. Applicant points out to col. 1, paragraphs 6 and 7 and argues that at these locations, the reference only teaches that cytostatic agents may exhibit greater efficacy in combination with

Ginkgo flavonoglycosides. Applicant argues that DE stresses the importance of administration of ginkgolides before the dose of the chemotherapeutic agents and that DE teaches high amplification of the tumor growth-inhibiting effect of cytostatic chemotherapeutic agents can be achieved by multiple prior administration of ginkgolides. These arguments are not found to be persuasive since instant claim language 'comprising' does not exclude the other anti-cancer agents in the references. Furthermore, it would appear that the references teach synergism of the extract and the other anti-cancer agents and this implies that each agent has some activity by itself and

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when combined, they show an enhanced activity. This is evident from claim 1 in EP and DE where only the extract for the treatment of metastatic cancer is recited. Applicant's arguments with regard to both references fail to teach that over expression of PBR is a distinguishable and testable attribute of cancer cells that may be used to determine which patients may be most amenable to treatment with Ginkgo extract containing GKB or with isolated GKB, the examiner points out that instant claims are drawn to 'a method of combating cancer which is characterized by an over-expression of peripheral-type benzodiazepine receptor protein (PBR protein)' and not to 'a method of interaction of Ginkgo extract containing GKB or isolated GKB with peripheral-type benzodiazepine receptor protein' and applicant has not shown that the cancer taught by the prior art does not have peripheral-type benzodiazepine receptor protein. As already pointed out, the mechanism by which GKB or extract containing GKB acts to have an effect on cancer cells has no significance.

The newly added claim 26 is included in this rejection since it is a composition claim claiming the Ginkgo biloba extract in an effective amount limitation. Applicant has not shown that the amount in the references is not an effective amount.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-3, 5-9, 12-13 and 15-24 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Fogarty 6,316,690.

Fogarty discloses the anti-tumor activity of Ginkgo biloba extract is known in the art. The tumors discussed in specific include hepatic, colon, leukemia, lymphoma, glioma, breast, prostate, pancreas, bladder, melanoma and lung (col. 12, line 44 through col. 13, line 27).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Fogarty makes a sweeping statement that a variety of herbs and Chinese medicines have been identified for having anti-tumor activity and that neither Fogarty itself nor a single reference cited by Fogarty recites treatment of cancer with Ginkgo biloba extracts or with isolated GKB. This argument is not persuasive. Fogarty teaches anti-tumor activity of the extracts of Ginkgo Biloba leaf itself in Table 2 on col. 13. Fogarty also states on col. 12, line 46 et seq., that "Those in Table 2 have activity against a variety of cancer types, which includes hepatic, colon, leukemia, lymphoma, glioma, breast, prostate, pancreas, bladder, melanoma and lung". Applicant's argument that Fogarty fails to teach or suggest to use a Ginkgo extract containing GKB or GKB to combat cancer cells characterized by an over-expression of PBR are similar to those raised for the rejections over DE and EP and these have been addressed above.

The newly added claim 26 is included in this rejection since it is a composition claim claiming the Ginkgo biloba extract in an effective amount limitation. Applicant has not shown that the amount in the references is not an effective amount.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-3, 5-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fogarty cited above.

Fogarty teaches a transgenic *Drosophila melanogaster* as the model to predict the ability of a compound's effectiveness in the treatment of cancer. One of the ingredients used by Fogarty is Ginkgo biloba extract. Based on this model taught by Fogarty combined with the art known anti-tumor activity of Ginkgo biloba extracts also taught by Fogarty, it would have been obvious to one of ordinary skill in the art to use Ginkgo extracts to treat various forms of cancer, with a reasonable expectation of success.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant points out col. 3, lines 35-38 of Fogarty and argue that at this location Fogarty states that a critical feature of the subject animals is that they are transgenic for a particular gene which is spatially expressed in a manner sufficient to result in the desired neoplastic phenotype. Applicant further argues that Fogarty provides no evidence that the teachings of their model system function in a similar

manner when the tumor, in any organism lacks this critical transgenic feature and that Fogarty does not teach or suggest that tumor cells may be characterized by an over expression of PBR. These arguments are not persuasive since instant claims are drawn to a method of combating cancer and not to a model system or to 'a method of interaction of Ginkgo extract containing GKB or isolated GKB with peripheral-type benzodiazepine receptor protein'. Fogarty does teach the anti-tumor activity of extracts from leaves of Ginkgo biloba based on the model and therefore, one of ordinary skill in the art would be motivated to use these extracts to any cancer with a reasonable expectation of success. Instant specification contains no data on the in vivo applicability of these extracts on various types of cancer as claimed.

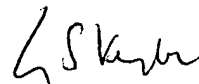
8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK